10/532296

PCT/IB03/04677

IB03/4677

सत्यमेव जयते

INTELLECTUAL PROPERTY INDIA

GOVERNMENT OF INDIA
MINISTRY OF COMMERCE & INDUSTRY,
PATENT OFFICE, DELHI BRANCH,
W - 5, WEST PATEL NAGAR,
NEW DELHI - 110 008.

PRIORITY DOCUMENT

SUBMITTED OR TRANSMITTED IN COMPLIANCE WITH RULE 17.1(a) OR (b)

I, the undersigned being an officer duly authorized in accordance with the provision of the Patent Act, 1970 hereby certify that annexed hereto is the true copy of the ***Application*** *and* ***Provisional Specification*** *filed in connection with Application for Patent No.**1056/Del/02** dated 22nd **October 2002.***

Witness my hand this 26th day of March 2004.

(S.K. PANGASA)
Assistant Controller of Patents & Designs

FORM 1

1032 DEL 2002

22 OCT 2002

A61K 9/00
A61K 31/00

THE PATENTS ACT, 1970
(39 of 1970)

APPLICATION FOR GRANT OF A PATENT

(See Sections 7, 54 and 135 and rule 33A)

1 We, **RANBAXY LABORATORIES LIMITED**, a Company incorporated under the Companies Act, 1956, Corporate Office at 19, Nehru Place, New Delhi - 110 019, India

2. hereby declare –

(a) that we are in possession of an invention titled **"RETARD RELEASE FORMULATIONS OF ALFUZOSIN HYDROCHLORIDE "**.

(b) that the Provisional Specification relating to this invention is filed with this application.

(c) that there is no lawful ground of objection to the grant of a patent to us.

3. Further declare that the inventors for the said invention are

a. NARAYANAN BADRI VISWANATHAN

b. RAJEEV SINGH RAGHUVANSHI

c. ASHOK RAMPAL

of Ranbaxy Laboratories Limited, Plot No. 20, Sector-18, Udyog Vihar Industrial Area, Gurgaon – 122001 (Haryana), India, all Indian Nationals.

4. That we are the assignee or legal representatives of the true and first inventors.

5. That our address for service in India is as follows:

DR. B. VIJAYARAGHAVAN
Associate Director – Intellectual Property
Ranbaxy Laboratories Limited
Plot No.20, Sector – 18,
Udyog Vihar Industrial Area,
Gurgaon – 122001 (Haryana), INDIA.
Tel. No. (91-124) 6343126; 6342001 – 10; 8912501-10
Fax No. (91-124) 6342027

6. Following declaration was given by the inventors in the convention country:

We, NARAYANAN BADRI VISWANATHAN, RAJEEV SINGH RAGHUVANSHI, ASHOK RAMPAL of Ranbaxy Laboratories Limited, Plot No. 20, Sector – 18, Udyog Vihar Industrial Area, Gurgaon–122001 (Haryana), India, all Indian Nationals, the true and first inventors for this invention in the convention country declare that the applicants herein, **Ranbaxy Laboratories Limited**, 19, Nehru Place, New Delhi - 110 019, India, is our assignee or legal representative.

a. Narayanan Badri Viswanathan

(NARAYANAN BADRI VISWANATHAN)

b. Rajeev Singh

(RAJEEV SINGH RAGHUVANSHI)

c.

(ASHOK RAMPAL)

7. That to the best of our knowledge, information and belief the fact and matters stated herein are correct and that there is no lawful ground of objection to the grant of patent to us on this application.

8. Followings are the attachment with the application:

a. Provisional Specification (3 copies)
b. Drawings (3 copies)
c. Statement and Undertaking on FORM – 3
d. Fee Rs.5,000/- (Rupees Five Thousand only..) in cheque bearing No. 684469 dated **13.09.2002** on **ANZ Grindlays Bank, New Delhi.**

We request that a patent may be granted to us for the said invention.

Dated this **21ST** day of **OCTOBER, 2002.**

For Ranbaxy Laboratories Limited

(SUSHIL KUMAR PATAWARI)
COMPANY SECRETARY

1068-2

22 OCT 2002

FORM 2

The Patents Act, 1970
(39 of 1970)

PROVISIONAL SPECIFICATION
(See Section 10)

RETARD RELEASE FORMULATIONS OF ALFUZOSIN HYDROCHLORIDE

RANBAXY LABORATORIES LIMITED
19, NEHRU PLACE, NEW DELHI - 110019
(A Company incorporated under the Companies Act, 1956)

The following specification particularly describes and ascertains the nature of this invention and the manner in which it is to be performed:

Alfuzosin belongs to the chemical class of 4-amino-6,7-dimethoxyquinazol-2-yl-alkylenediamines. It is used for the treatment of benign prostatic hypertrophy and hypertension. The retard release formulations provide various advantages over the conventional multiple dosing vis-a-vis better patient compliance, reduced fluctuations of plasma drug levels, reduced toxicity etc.

The present invention relates to the retard release oral dosage form, comprising a therapeutically effective amount of Alfuzosin or pharmaceutically accepted salt, solvate, enantiomers or mixtures thereof, in a controlled release matrix such that said dosage form provides a therapeutic effect for extended period of time after oral administration. The retard release dosage form of the present invention comprises Alfuzosin or pharmaceutically accepted salts, solvates or enantiomers or mixtures thereof, one or more excipients selected from binders, disintegrants, lubricants or coating agents and release retarding polymers selected from hydroxypropyl methylcellulose, hydroxypropyl cellulose, polymers or copolymers of acrylic acid and equivalents thereof. The said polymers, for the purpose of present invention, can be classified based on their solubility and pH dependent release. The retard release formulation of the present invention releases the active ingredient over extended period of time after oral administration. The said formulation can also be prepared in order to obtain the zero order release profile.

The following examples are exemplary only and should not be construed to limit the scope of the invention in any way.

EXAMPLE 1

Alfuzosin Hydrochloride Retard Release Tablets – 10mg

The ingredients used for the preparation of retard release formulation of Alfuzosin hydrochloride are listed below.

S.N.	Ingredient	%
1	Alfuzosin Hydrochloride	1.5-5.0
2	Hydroxypropylmethyl cellulose HPMC (Methocel K100M CR)	5-50
3	Hydroxypropyl cellulose HPC (M)	5-50
4	Eudragit L 100 55	1-35
5	Lactose/Microcrystalline cellulose/Dicalcium phosphate	15-70
6	Magnesium Stearate	0-5
7	Talc	0-5
8	Colloidal silicon dioxide (Aerosil 200)	0-5
	Total Core Tablet Weight	100
	Coating OPADRY White	0.5-3.0

Direct compression method:

The drug and other excipients are mixed to obtain a blend. The blend obtained is then lubricated and compressed into tablets. The said tablets may be optionally coated.

EXAMPLE 2

Alfuzosin Hydrochloride Retard Release Tablets – 10mg

The ingredients used for the preparation of retard release formulation of Alfuzosin hydrochloride are listed below.

S.N.	Ingredient	%
1	Alfuzosin Hydrochloride	1.5-5.0
2	Hydroxypropylmethyl cellulose HPMC (Methocel K100M CR)	5-50
3	Hydroxypropyl cellulose HPC (M)	5-50
4	Eudragit L-100 55	1-35
5	Lactose/Microcrystalline cellulose/Dicalcium phosphate	15-70
6	Magnesium Stearate	0-5
7	Talc	0-5
8	Colloidal silicon dioxide (Aerosil 200)	0-5
9	Polyvinylpyrrolidone	0-10
	Total Core Tablet Weight	100
	Coating OPADRY White	0.5-3.0

Wet granulation method:

The drug is geometrically mixed with other ingredients and granulated with a binder solution (solution of polyvinylpyrrolidone or such like) to obtain granules. The said granules are then dried, sifted, lubricated and compressed into tablets or filled into capsules. The tablets are optionally coated.

The representative dissolution profile, without limiting the scope of the invention in any way, of the retard release formulations of Alfuzosin hydrochloride is given below.

Dissolution profile of uncoated tablets using USP-2 apparatus, 500ml of 0.01N HCl at 100 rpm.

Time hrs	% released
0	0
1	17
2	26
4	39
8	61
12	77
16	88
20	94
24	96

As used in this specification the word retard release has its conventional meaning and may also be referred to as controlled, prolonged, extended or sustained release. The inert excipients such as binders, diluents, lubricants, fillers or coating agents may be replaced by suitable equivalents as per the scope of the invention.

Dated this 21ST day of **October, 2002.**

For Ranbaxy Laboratories Limited

(Sushil Kumar Patawari)
Company Secretary